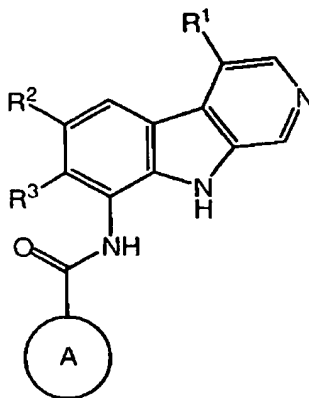


Practitioner's Docket No. MPI03-043P1RNMIn the Claims:RECEIVED
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1. (Original) A compound of formula 1:



I

or a pharmaceutically acceptable salt thereof, wherein:

Ring A is selected from the group consisting of:

(a) a pyridinyl or pyrimidinyl ring that is substituted by (i) $-\text{CH}_2\text{C}(\text{O})-\text{G}$ and 0-1 R^{6a} or (ii) 1-2 R^{6a} , and

(b) a morpholinyl, piperidinyl, piperazinyl, pyrrolidinyl, pyranyl, tetrahydrofuranyl, cyclohexyl, cyclopentyl or thiomorpholinyl ring that is substituted by (i) $-\text{C}(\text{R}^9)_3$, $-\text{W}-\text{G}$, or $-\text{G}$, (ii) 0-4 R^{6b} and (iii) 0-1 oxo groups on a ring carbon or 0-2 oxo groups on a ring sulfur;

each R^{6a} is independently selected from C_{1-6} aliphatic, halo, alkoxy, or amino;

each R^{6b} is independently selected from C_{1-3} aliphatic or $-\text{N}(\text{R}^7)_2$, and two R^{6b} on the same or an adjacent carbon optionally are taken together with the intervening carbon(s) to form a 5-6 membered ring having 1-2 ring heteroatoms selected from N, O or S;

W is $-\text{Q}-$, $-\text{Q}-\text{C}(\text{O})-$, $-\text{C}(\text{R}^9)_2-\text{C}(\text{R}^9)(\text{R}^{12})-$, or $-\text{C}(\text{R}^9)_2-[\text{C}(\text{R}^9)(\text{R}^{12})]_2-$;

Q is $-\text{C}(\text{R}^9)_2-$ or $-\text{C}(\text{R}^9)_2\text{C}(\text{R}^9)-$;

G is $-\text{OH}$, $-\text{NR}^4\text{R}^5$, $-\text{N}(\text{R}^9)\text{CONR}^4\text{R}^5$, $-\text{N}(\text{R}^9)\text{SO}_2(\text{C}_{1-3}\text{ aliphatic})$, $-\text{N}(\text{R}^9)\text{COCF}_3$, $-\text{N}(\text{R}^9)\text{CO}(\text{C}_{1-6}\text{ aliphatic})$, $-\text{N}(\text{R}^9)\text{CO}(\text{heterocyclyl})$, $-\text{N}(\text{R}^9)\text{CO}(\text{heteroaryl})$, $-\text{N}(\text{R}^9)\text{CO}(\text{aryl})$, a 3-7 membered heterocyclyl ring, or a 5-6 membered heteroaryl, wherein each of the heteroaryl, aryl and heterocyclyl moieties of G is optionally substituted by 1-3 R^{10} ;

R^1 is hydrogen, halo, C_{1-3} aliphatic, amino, cyano, $(\text{C}_{1-3}\text{ alkyl})_{1-2}$ amino, C_{1-3} alkoxy, $-\text{CONH}_2$, $-\text{NHCOCF}_3$, or $-\text{CH}_2\text{NH}_2$;

R^2 is hydrogen, halo, C_{1-3} aliphatic, $-\text{CF}_3$;

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R^3 is hydrogen, halo, C_{1-6} aliphatic, C_{1-6} haloalkyl, C_{1-6} alkoxy, hydroxy, amino, cyano, or $(C_{1-6} \text{ alkyl})_{1-2}$ amino;

R^4 is hydrogen, 3-7 membered heterocyclyl, or C_{1-6} aliphatic;

R^5 is hydrogen, C_{1-6} aliphatic group or a 3-7 membered heterocyclic ring having 1-2 ring heteroatoms selected from N, O, or S, wherein R^5 is optionally substituted by halo, $-OR^7$, $-CN$, $-SR^8$, $-S(O)_2R^8$, $-S(O)_2N(R^7)_2$, $-C(O)R^7$, $-CO_2R^7$, $-N(R^7)_2$, $-C(O)N(R^7)_2$, $-N(R^7)C(O)R^7$, $-N(R^7)CO_2R^8$, or $-N(R^7)C(O)N(R^7)_2$;

each R^7 is independently selected from hydrogen or C_{1-4} aliphatic, or two R^7 on the same nitrogen atom are taken together with the nitrogen to form a 5-6 membered heteroaryl or heterocyclyl ring;

each R^8 is independently selected from C_{1-4} aliphatic;

each R^9 is independently selected from hydrogen or C_{1-3} aliphatic;

each R^{10} is independently selected from oxo, $-R^{11}$, $-T-R^{11}$, or $-V-T-R^{11}$;

each R^{11} is independently selected from C_{1-6} aliphatic, halo, $-S(O)_2N(R^7)_2$, $-OR^7$, $-CN$, $-SR^8$, $-S(O)_2R^8$, $-C(O)R^7$, $-CO_2R^7$, $-N(R^7)_2$, $-C(O)N(R^7)_2$, $-N(R^7)C(O)R^7$, $-N(R^7)CO_2R^7$, or $-N(R^7)C(O)N(R^7)_2$;

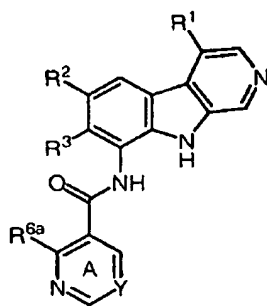
T is a straight or branched C_{1-4} alkylene chain;

V is $-O-$, $-N(R^7)-$, $-S-$, $-S(O)-$, $-S(O)_2-$, $-C(O)-$, or $-CO_2-$; and

R^{12} is hydrogen or an amino acid side chain.

2. (Original) The compound of claim 1 where Ring A is a 3-pyridinyl or 5-pyrimidinyl ring substituted by 1-2 R^{6a} groups.

3. (Original) The compound of claim 2 having formula II-C:



II-C

wherein:

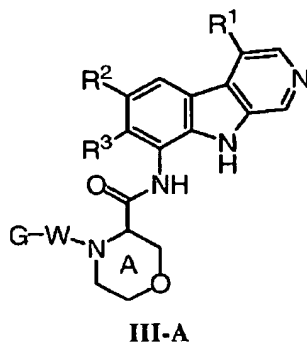
Y is N or CH;

R^1 is hydrogen, halo, C_{1-3} aliphatic, amino, cyano, $(C_{1-3} \text{ alkyl})_{1-2}$ amino, C_{1-3} alkoxy, $-CONH_2$, $-NHCOCF_3$, or $-CH_2NH_2$;

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- R^2 is hydrogen, halo, C_{1-3} aliphatic, $-CF_3$;
 R^3 is hydrogen, halo, C_{1-6} aliphatic, C_{1-6} haloalkyl, C_{1-6} alkoxy, hydroxy, amino, cyano, or $(C_{1-6}$ alkyl) $_{1-2}$ amino; and
 R^{6a} is selected from C_{1-6} aliphatic or halo.
4. (Original) The compound of claim 3 where R^{6a} is methyl.
5. (Original) The compound of claim 4 where R^1 is hydrogen, methyl, amino or fluoro; R^2 is hydrogen or halo; and R^3 is hydrogen, halo or C_{1-4} alkoxy.
6. (Original) The compound of claim 5 where Y is CH.
7. (Original) The compound of claim 5 where Y is N.
8. (Original) The compound of claim 1 where Ring A is selected from morpholinyl, piperidinyl, piperazinyl, pyrrolidinyl, pyranyl, tetrahydrofuranyl, cyclohexyl, cyclopentyl or thiomorpholinyl and where Ring A is substituted by (i) $-C(R^9)_3$ or $-W-G$, (ii) 0-4 R^{6b} and (iii) 0-1 oxo groups on a ring carbon or 0-2 oxo groups on a ring sulfur.
9. (Original) The compound of claim 8 where the $-W-G$ or $-C(R^9)_3$ substituent on Ring A is ortho to the position where the beta-carboline portion is attached.
10. (Original) A compound of formula III-A:



or a pharmaceutically acceptable salt thereof, wherein:

Ring A is substituted by 0-4 R^{6b} ;

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each R^{6b} is independently selected from C_{1-3} aliphatic or $-N(R^7)_2$, and two R^{6b} on the same or an adjacent carbon optionally are taken together with the intervening carbon(s) to form a 5-6 membered ring having 1-2 ring heteroatoms selected from N, O or S;

W is $-Q-$, $-Q-C(O)-$, $-C(R^9)_2-C(R^9)(R^{12})-$, or $-C(R^9)_2-[C(R^9)(R^{12})]_2-$;

Q is $-C(R^9)_2-$ or $-C(R^9)_2C(R^9)_2-$;

G is $-OH$, $-NR^4R^5$, $-N(R^9)CONR^4R^5$, $-N(R^9)SO_2(C_{1-3} \text{ aliphatic})$, $-N(R^9)COCF_3$, $-N(R^9)CO(C_{1-6} \text{ aliphatic})$, $-N(R^9)CO(\text{heterocyclyl})$, $-N(R^9)CO(\text{heteroaryl})$, $-N(R^9)CO(\text{aryl})$, a 3-7 membered heterocyclyl ring, or a 5-6 membered heteroaryl, wherein each of the heteroaryl, aryl and heterocyclyl moieties of G is optionally substituted by 1-3 R^{10} ;

R^1 is hydrogen, halo, C_{1-3} aliphatic, amino, cyano, $(C_{1-3} \text{ alkyl})_{1-2}$ amino, C_{1-3} alkoxy, $-CONH_2$, $-NHCOCF_3$, or $-CH_2NH_2$;

R^2 is hydrogen, halo, C_{1-3} aliphatic, $-CF_3$;

R^3 is hydrogen, halo, C_{1-6} aliphatic, C_{1-6} haloalkyl, C_{1-6} alkoxy, hydroxy, amino, cyano, or $(C_{1-6} \text{ alkyl})_{1-2}$ amino;

R^4 is hydrogen, 5-6 membered heterocyclyl, or C_{1-6} aliphatic;

R^5 is hydrogen, C_{1-6} aliphatic group or a 5-6 membered heterocyclic ring having 1-2 ring heteroatoms selected from N, O, or S, wherein R^5 is optionally substituted by halo, $-OR^7$, $-CN$, $-SR^8$, $-S(O)_2R^8$, $-S(O)_2N(R^7)_2$, $-C(O)R^7$, $-CO_2R^7$, $-N(R^7)_2$, $-C(O)N(R^7)_2$, $-N(R^7)C(O)R^7$, $-N(R^7)CO_2R^8$, or $-N(R^7)C(O)N(R^7)_2$;

each R^7 is independently selected from hydrogen or C_{1-4} aliphatic, or two R^7 on the same nitrogen atom are taken together with the nitrogen to form a 5-6 membered heteroaryl or heterocyclyl ring;

each R^8 is independently selected from C_{1-4} aliphatic;

each R^9 is independently selected from hydrogen or C_{1-3} aliphatic;

each R^{10} is independently selected from oxo, $-R^{11}$, $-T-R^{11}$, or $-V-T-R^{11}$;

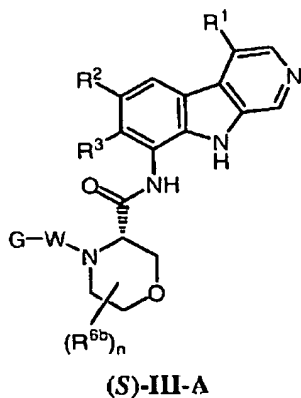
each R^{11} is independently selected from C_{1-6} aliphatic, halo, $-S(O)_2N(R^7)_2$, $-OR^7$, $-CN$, $-SR^8$, $-S(O)_2R^8$, $-C(O)R^7$, $-CO_2R^7$, $-N(R^7)_2$, $-C(O)N(R^7)_2$, $-N(R^7)C(O)R^7$, $-N(R^7)CO_2R^7$, or $-N(R^7)C(O)N(R^7)_2$;

T is a straight or branched C_{1-4} alkylene chain;

V is $-O-$, $-N(R^7)-$, $-S-$, $-S(O)-$, $-S(O)_2-$, $-C(O)-$, or $-CO_2-$; and

R^{12} is hydrogen or an amino acid side chain.

11. (Original) The compound of claim 10 having the formula (S)-III-A:

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where n is 0-4 and R¹, R², R³, W, G and R^{6b} are as defined in claim 10.

12. (Original) The compound of claim 11 where:

R¹ is hydrogen, halo, methyl or amino;

R² is hydrogen, methyl or halo;

R³ is hydrogen, halo, alkoxy, or (C₁₋₆ aliphatic)₂ amino;

n is 0-2;

R^{6b} is C₁₋₃ aliphatic;

W is -Q-, -Q-C(O)-, -C(R⁹)₂-C(R⁹)(R¹²)-, or -C(R⁹)₂-[C(R⁹)(R¹²)]₂-;

Q is -C(R⁹)₂- or -C(R⁹)₂C(R⁹)₂-;

G is -NR⁴R⁵, -N(R⁹)C(O)NR⁴R⁵, -N(R⁹)SO₂(C₁₋₃ aliphatic), -N(R⁹)C(O)CF₃, -N(R⁹)CO(C₁₋₆ aliphatic), and -N(R⁹)CO(heterocyclyl), -N(R⁹)CO(heteroaryl), -N(R⁹)CO(aryl), a 5-6 membered heterocyclyl ring, or a 5-6 membered heteroaryl, wherein each of the heteroaryl, aryl and heterocyclyl moieties of G is optionally substituted by 1-3 R¹⁰;

R⁴ is hydrogen or C₁₋₆ aliphatic;

R⁵ is hydrogen or a C₁₋₆ aliphatic group that is optionally substituted by halo, -OR⁷, -CN, -SR⁸, -S(O)₂R⁸, -S(O)₂N(R⁷)₂, -C(O)R⁷, -CO₂R⁷, -N(R⁷)₂, -C(O)N(R⁷)₂, -N(R⁷)C(O)R⁷, -N(R⁷)CO₂R⁸, or -N(R⁷)C(O)N(R⁷)₂;

each R⁷ is independently selected from hydrogen or C₁₋₄ aliphatic, or two R⁷ on the same nitrogen atom are taken together with the nitrogen to form a 5-6 membered heteroaryl or heterocyclyl ring;

each R⁸ is independently selected from C₁₋₄ aliphatic;

R⁹ is hydrogen;

each R¹⁰ is independently selected from oxo, R¹¹, T-R¹¹, or V-T-R¹¹;

each R¹¹ is independently selected from C₁₋₆ aliphatic, halo, -S(O)₂N(R⁷)₂, -OR⁷, -CN, -SR⁸, -S(O)₂R⁸, -C(O)R⁷, -CO₂R⁷, -N(R⁷)₂, -C(O)N(R⁷)₂, -N(R⁷)C(O)R⁷, -N(R⁷)CO₂R⁷, or -N(R⁷)C(O)N(R⁷)₂;

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T is a straight or branched C₁₋₄ alkylene chain;

V is -O-, -N(R⁷)-, -S-, -S(O)-, -S(O)₂-, -C(O)-, or -CO₂-; and

R¹² is hydrogen, C₁₋₆ aliphatic, substituted or unsubstituted phenyl, or substituted or unsubstituted benzyl.

13. (Original) The compound of claim 12 where:

R¹ is hydrogen, methyl, fluoro or amino;

R² is chloro;

R³ is hydrogen or alkoxy;

n is zero or 2;

R^{6b} is methyl;

W is -Q-, -Q-C(O)- or -C(R⁹)₂-C(R⁹)(R¹²)-;

Q is -C(R⁹)₂- or -C(R⁹)₂C(R⁹)₂-;

G is -NR⁴R⁵, -N(R⁹)C(O)NR⁴R⁵, -N(R⁹)C(O)CF₃, -N(R⁹)CO(C₁₋₆ aliphatic), and -N(R⁹)CO(heterocyclyl), -N(R⁹)CO(heteroaryl), a 5-6 membered heterocyclyl ring, or a 5-6 membered heteroaryl, wherein each of the heteroaryl and heterocyclyl moieties of G is optionally substituted by 1-3 R¹⁰;

R⁴ is hydrogen or C₁₋₆ aliphatic;

R⁵ is hydrogen or C₁₋₆ aliphatic;

each R⁷ is independently selected from hydrogen or C₁₋₄ aliphatic, or two R⁷ on the same nitrogen atom are taken together with the nitrogen to form a 5-6 membered heteroaryl or heterocyclyl ring;

each R⁸ is independently selected from C₁₋₄ aliphatic;

R⁹ is hydrogen;

each R¹⁰ is independently selected from oxo, R¹¹, T-R¹¹, or V-T-R¹¹;

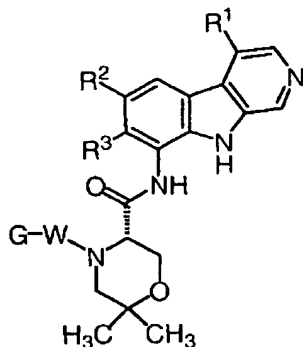
each R¹¹ is independently selected from C₁₋₆ aliphatic, halo, -S(O)₂N(R⁷)₂, -OR⁷, -CN, -SR⁸, -S(O)₂R⁸, -C(O)R⁷, -CO₂R⁷, -N(R⁷)₂, -C(O)N(R⁷)₂, -N(R⁷)C(O)R⁷, -N(R⁷)CO₂R⁷, or -N(R⁷)C(O)N(R⁷)₂;

T is a straight or branched C₁₋₄ alkylene chain;

V is -O-, -N(R⁷)-, -S-, -S(O)-, -S(O)₂-, -C(O)-, or -CO₂-; and

R¹² is hydrogen, C₁₋₆ aliphatic, phenyl, or benzyl.

14. (Original) A compound of formula (S)-III-A':

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(S)-III-A'

or a pharmaceutically acceptable salt thereof, wherein:

R¹ is hydrogen, methyl, fluoro or amino;

R² is chloro;

R³ is hydrogen or alkoxy;

W is -Q-, -Q-C(O)- or -C(R⁹)₂-C(R⁹)(R¹²)-;

Q is -C(R⁹)₂- or -C(R⁹)₂C(R⁹)₂-;

G is -NR⁴R⁵, -N(R⁹)C(O)NR⁴R⁵, -N(R⁹)C(O)CF₃, -N(R⁹)CO(C₁₋₆ aliphatic), and -N(R⁹)CO(heterocyclyl), -N(R⁹)CO(heteroaryl), a 5-6 membered heterocyclyl ring, or a 5-6 membered heteroaryl, wherein each of the heteroaryl and heterocyclyl moieties of G is optionally substituted by 1-3 R¹⁰;

R⁴ is hydrogen or C₁₋₆ aliphatic;

R⁵ is hydrogen or C₁₋₆ aliphatic;

each R⁷ is independently selected from hydrogen or C₁₋₄ aliphatic, or two R⁷ on the same nitrogen atom are taken together with the nitrogen to form a 5-6 membered heteroaryl or heterocyclyl ring;

each R⁸ is independently selected from C₁₋₄ aliphatic;

R⁹ is hydrogen;

each R¹⁰ is independently selected from oxo, R¹¹, T-R¹¹, or V-T-R¹¹;

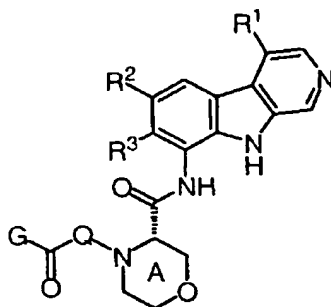
each R¹¹ is independently selected from C₁₋₆ aliphatic, halo, -S(O)₂N(R⁷)₂, -OR⁷, -CN, -SR⁸, -S(O)₂R⁸, -C(O)R⁷, -CO₂R⁷, -N(R⁷)₂, -C(O)N(R⁷)₂, -N(R⁷)C(O)R⁷, -N(R⁷)CO₂R⁷, or -N(R⁷)C(O)N(R⁷)₂;

T is a straight or branched C₁₋₄ alkylene chain;

V is -O-, -N(R⁷)-, -S-, -S(O)-, -S(O)₂-, -C(O)-, or -CO₂-; and

R¹² is hydrogen, C₁₋₆ aliphatic, phenyl, or benzyl.

15. (Original) The compound of claim 14 having the formula (S)-III-A-a:

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(S)-III-A-a

where R¹ is hydrogen, halo, methyl or amino;

R² is hydrogen, methyl or halo;

R³ is hydrogen, halo, alkoxy, or (C₁₋₆ aliphatic)₂ amino;

Ring A is substituted by 0-2 R^{6b};

R^{6b} is C₁₋₃ aliphatic;

Q is -C(R⁹)₂- or -C(R⁹)₂C(R⁹)₂-;

G is -NR⁴R⁵ or a substituted or unsubstituted 5-6 membered heterocyclyl ring;

R⁴ is hydrogen or C₁₋₆ aliphatic;

R⁵ is hydrogen or a C₁₋₆ aliphatic group that is optionally substituted by halo, -OR⁷, -CN, -SR⁸, -S(O)₂R⁸, -S(O)₂N(R⁷)₂, -C(O)R⁷, -CO₂R⁷, -N(R⁷)₂, -C(O)N(R⁷)₂, -N(R⁷)C(O)R⁷, -N(R⁷)CO₂R⁸, or -N(R⁷)C(O)N(R⁷)₂;

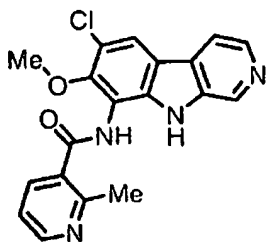
each R⁷ is independently selected from hydrogen or C₁₋₄ aliphatic, or two R⁷ on the same nitrogen atom are taken together with the nitrogen to form a 5-6 membered heteroaryl or heterocyclyl ring;

each R⁸ is independently selected from C₁₋₄ aliphatic; and

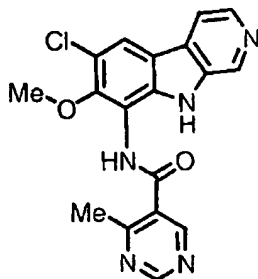
each R⁹ is independently hydrogen or C₁₋₃ aliphatic.

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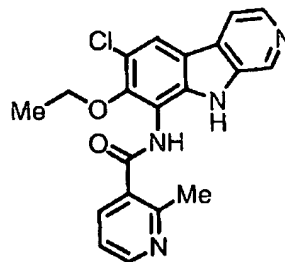
16. (Original) A compound selected from the group consisting of:



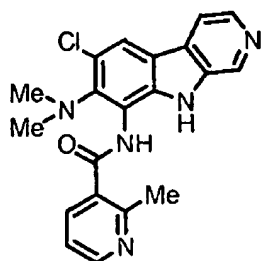
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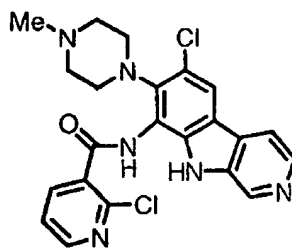
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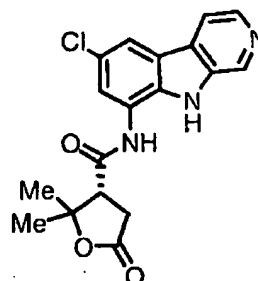
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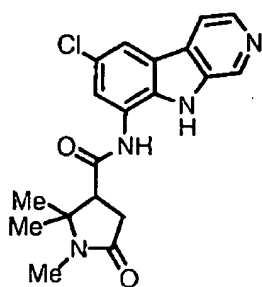
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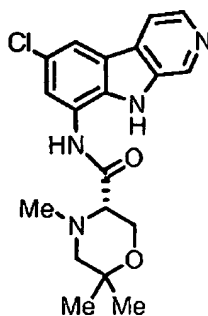
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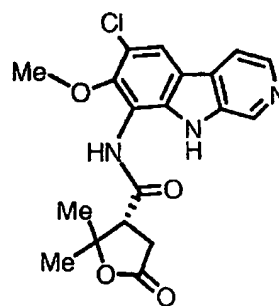
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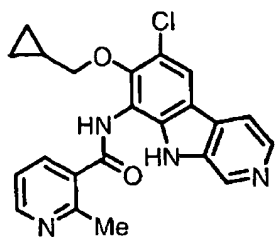
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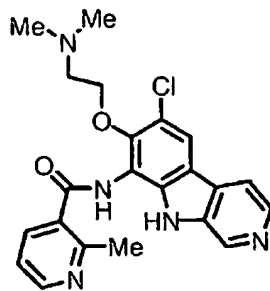
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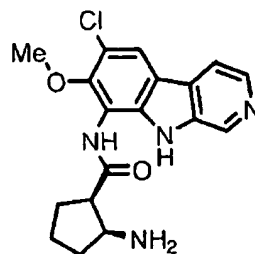
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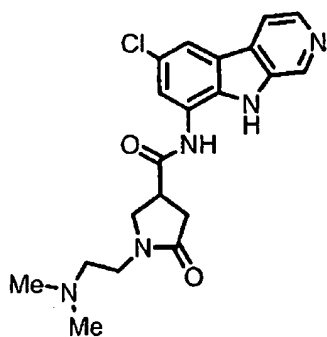
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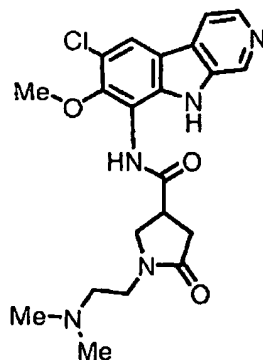
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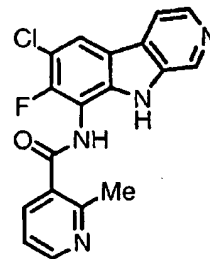
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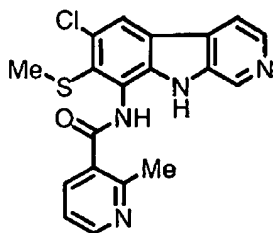
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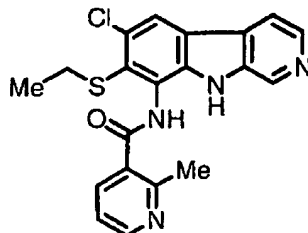
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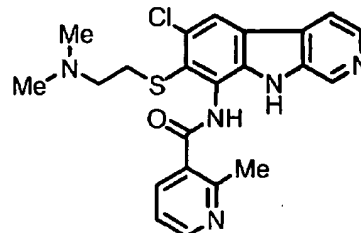
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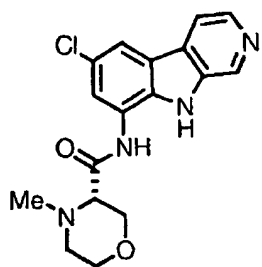
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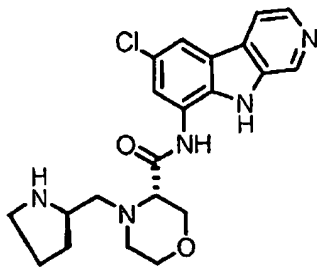
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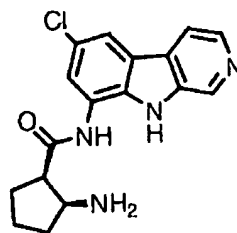
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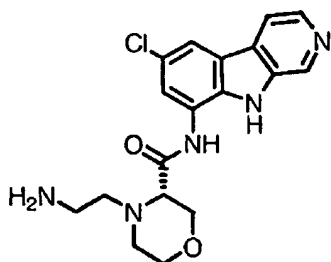
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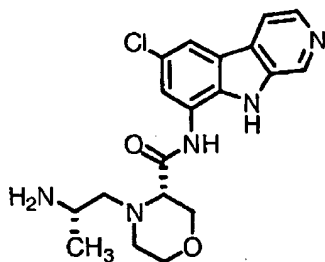
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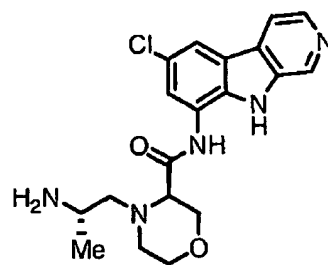
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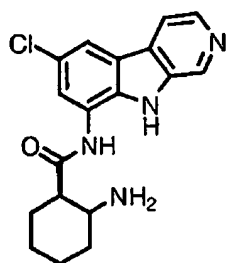
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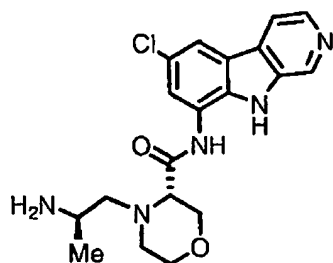
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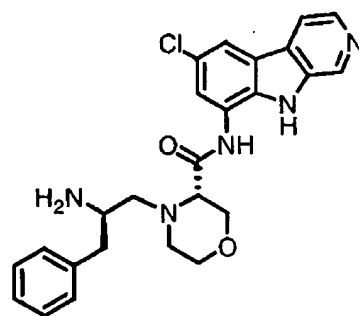
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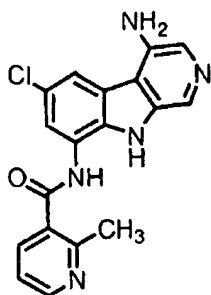
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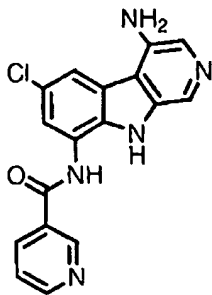
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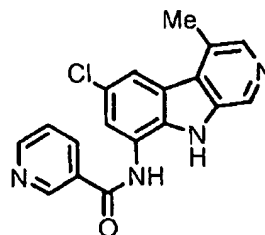
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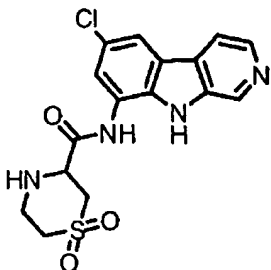
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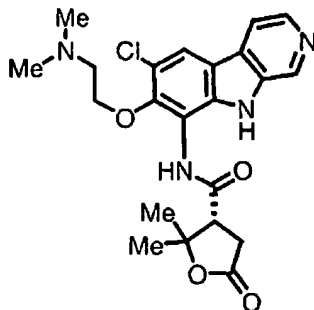
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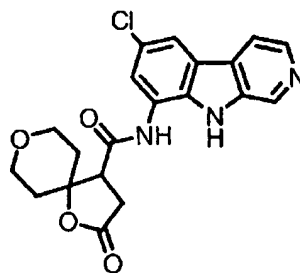
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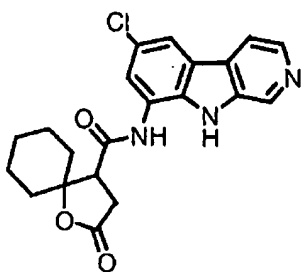
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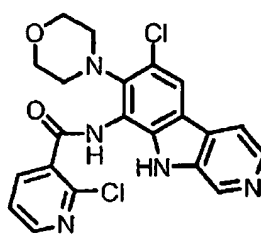
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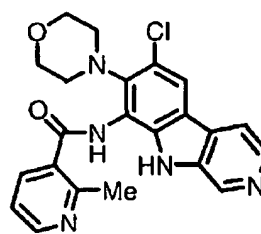
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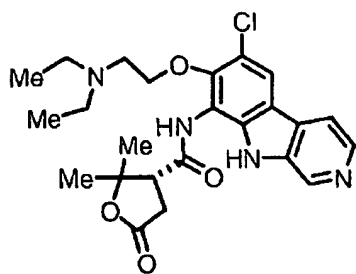
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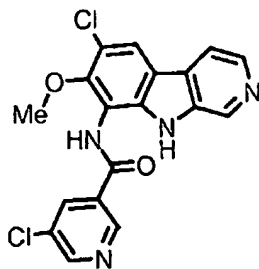
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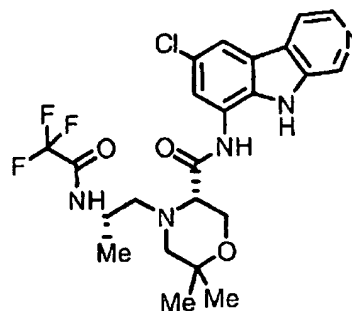
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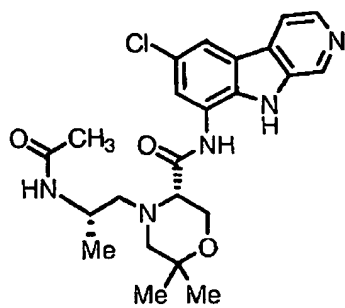
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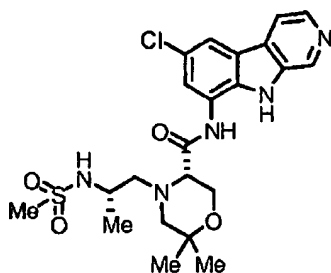
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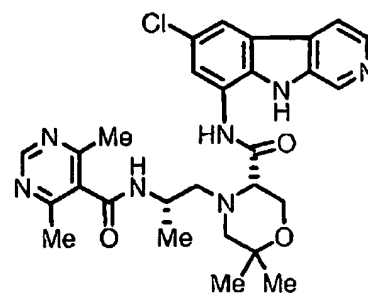
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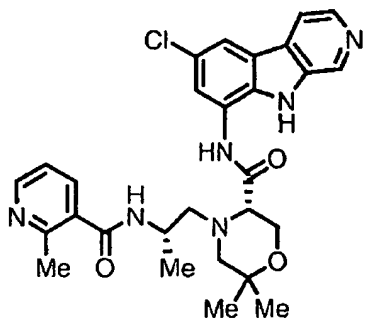
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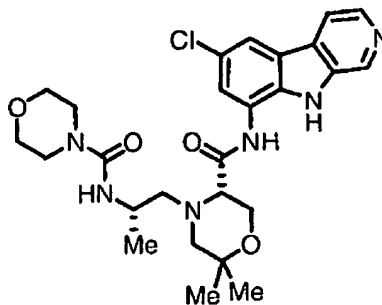
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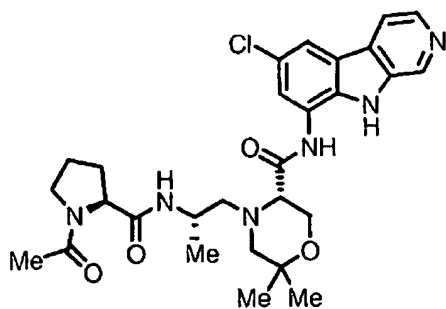
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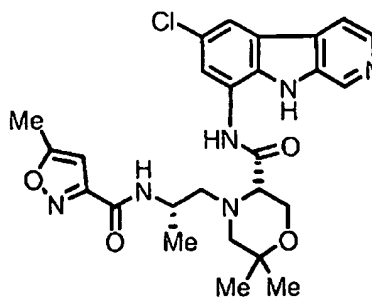
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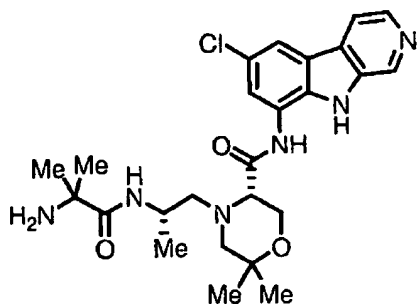
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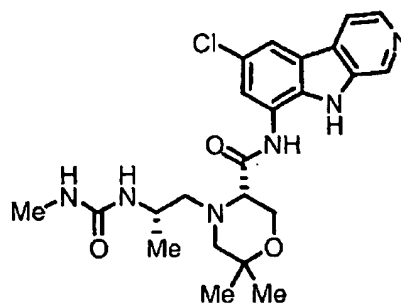
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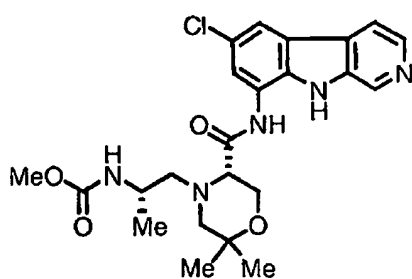
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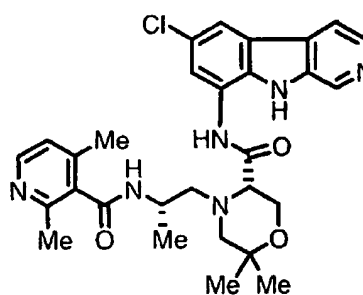
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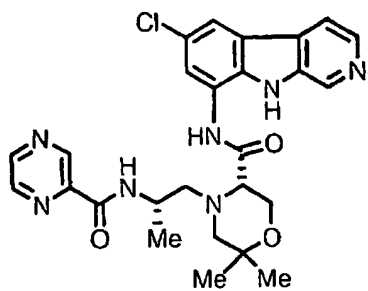
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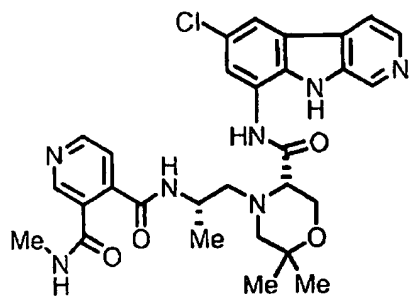
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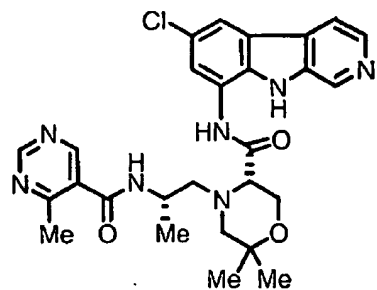
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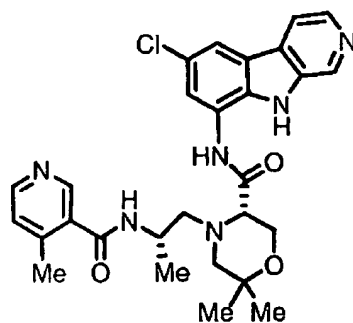
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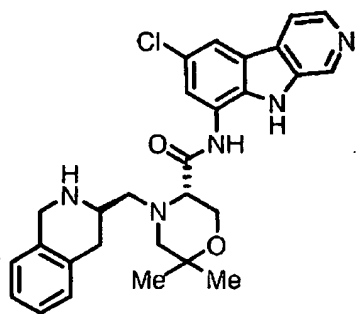
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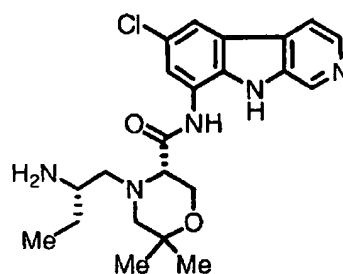
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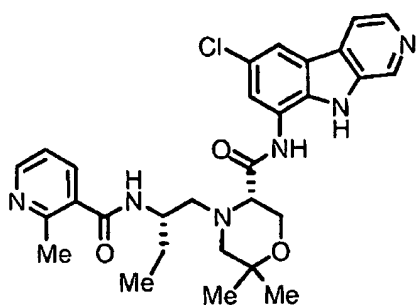
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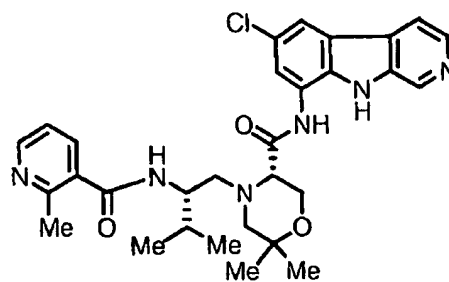
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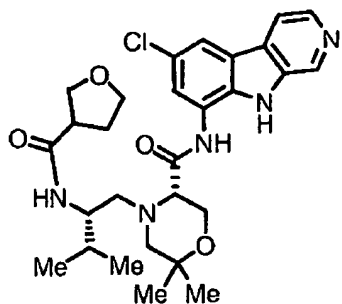
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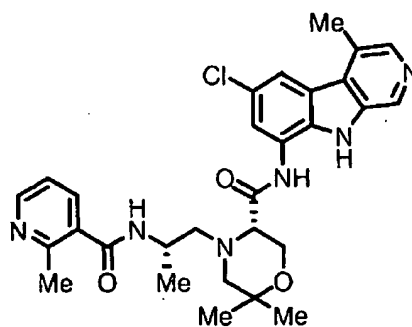
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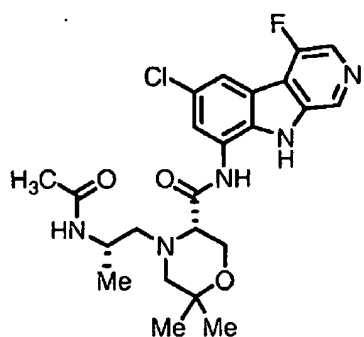
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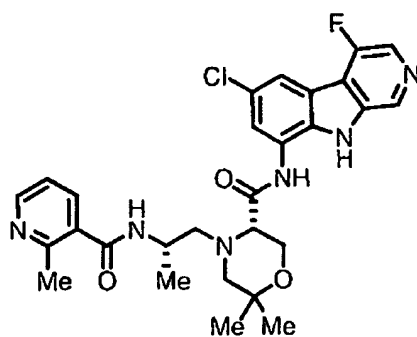
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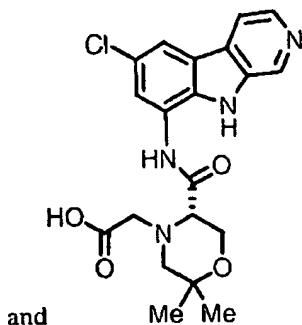


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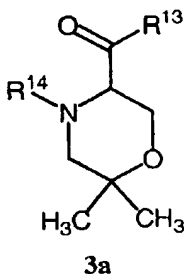
17. (Original) A pharmaceutical composition comprising a compound of claim 1 and a pharmaceutically acceptable carrier.
18. (Original) A pharmaceutical composition comprising a compound of claim 16 and a pharmaceutically acceptable carrier.
19. (Withdrawn) A method of treating an IKK-mediated disease comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 1.
20. (Withdrawn) The method of claim 19 wherein the disease is an inflammatory disease or an immune-related disease.
21. (Withdrawn) The method of claim 19 wherein the disease is selected from the group consisting of rheumatoid arthritis, asthma, psoriasis, psoriatic arthritis, chronic obstructive pulmonary disease, inflammatory bowel disease or multiple sclerosis.
22. (Withdrawn) The method of claim 19 wherein the disease is cancer.
23. (Withdrawn) The method of claim 22 wherein the cancer is selected from lymphoma, multiple myeloma, osteolytic bone metastasis, head or neck cancer, lung cancer, prostate cancer or pancreatic cancer.
24. (Withdrawn) The method of claim 23 wherein the cancer is a lymphoma.

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25. (Withdrawn) A method of inhibiting IKK in a patient in need thereof comprising administering to the patient a compound of claim 1.

26. (Withdrawn) A compound of formula 3a:



where R^{13} is halo, OH, OR^{15} , or a carboxylic acid protecting group;

R^{15} is an aliphatic, aryl, heteroaryl, aralkyl, or heteroaralkyl;

R^{14} is an amino protecting group, hydrogen or -W-G;

W is -Q-, -Q-C(O)-, -C(R^9)₂-C(R^9)(R^{12})-, or -C(R^9)₂-[C(R^9)(R^{12})]₂-;

Q is -C(R^9)₂- or -C(R^9)₂C(R^9)₂-;

G is -OH, -NR⁴R⁵, -N(R^9)CONR⁴R⁵, -N(R^9)SO₂(C₁₋₃ aliphatic), -N(R^9)COCF₃, -N(R^9)CO(C₁₋₆ aliphatic), -N(R^9)CO(heterocyclyl), -N(R^9)CO(heteroaryl), -N(R^9)CO(aryl), a 3-7 membered heterocyclyl ring, or a 5-6 membered heteroaryl, wherein each of the heteroaryl, aryl and heterocyclyl moieties of G is optionally substituted by 1-3 R^{10} ;

R^4 is hydrogen, 3-7 membered heterocyclyl, or C₁₋₆ aliphatic;

R^5 is hydrogen, C₁₋₆ aliphatic group or a 3-7 membered heterocyclic ring having 1-2 ring heteroatoms selected from N, O, or S, wherein R^5 is optionally substituted by halo, -OR⁷, -CN, -SR⁸, -S(O)₂R⁸, -S(O)₂N(R^7)₂, -C(O)R⁷, -CO₂R⁷, -N(R^7)₂, -C(O)N(R^7)₂, -N(R^7)C(O)R⁷, -N(R^7)CO₂R⁸, or -N(R^7)C(O)N(R^7)₂;

each R^7 is independently selected from hydrogen or C₁₋₄ aliphatic, or two R^7 on the same nitrogen atom are taken together with the nitrogen to form a 5-6 membered heteroaryl or heterocyclyl ring;

each R^8 is independently selected from C₁₋₄ aliphatic;

each R^9 is independently selected from hydrogen or C₁₋₃ aliphatic;

each R^{10} is independently selected from oxo, -R¹¹, -T-R¹¹, or -V-T-R¹¹;

each R^{11} is independently selected from C₁₋₆ aliphatic, halo, -S(O)₂N(R^7)₂, -OR⁷, -CN, -SR⁸, -S(O)₂R⁸, -C(O)R⁷, -CO₂R⁷, -N(R^7)₂, -C(O)N(R^7)₂, -N(R^7)C(O)R⁷, -N(R^7)CO₂R⁷, or -N(R^7)C(O)N(R^7)₂;

T is a straight or branched C₁₋₄ alkylene chain;

V is -O-, -N(R^7)-, -S-, -S(O)-, -S(O)₂-, -C(O)-, or -CO₂-; and

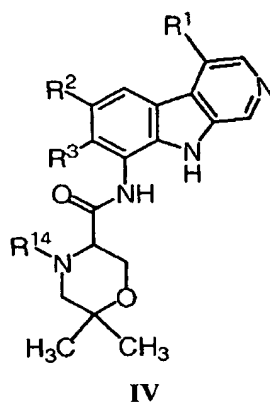
R^{12} is hydrogen or an amino acid side chain.

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27. (Withdrawn) The compound of claim 26 that is (S)-3a.

28. (Original) A compound of formula IV:



where R¹⁴ is an amino protecting group or hydrogen;

R¹ is hydrogen, halo, C₁₋₃ aliphatic, amino, cyano, (C₁₋₃ alkyl)₁₋₂ amino, C₁₋₃ alkoxy, -CONH₂, -NHCOCF₃, or -CH₂NH₂;

R² is hydrogen, halo, C₁₋₃ aliphatic, -CF₃; and

R³ is hydrogen, halo, C₁₋₆ aliphatic, C₁₋₆ haloalkyl, C₁₋₆ alkoxy, hydroxy, amino, cyano, or (C₁₋₆ alkyl)₁₋₂ amino.

29. (Original) The compound of claim 28 that is (S)-IV.

30. (New) A method of treating an inflammatory disease or an immune-related disease comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 1.

31. (New) The method of claim 30 wherein the disease is selected from rheumatoid arthritis, asthma, psoriasis, psoriatic arthritis, chronic obstructive pulmonary disease, inflammatory bowel disease or multiple sclerosis.

32. (New) A method of treating cancer comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 1.

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33. (New) The method of claim 32 wherein the cancer is selected from lymphoma, multiple myeloma, osteolytic bone metastasis, head or neck cancer, lung cancer, prostate cancer or pancreatic cancer.

34. (New) The method of claim 33 wherein the cancer is a lymphoma.